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# TYROSINE DERIVATIVES

## RELATED APPLICATIONS

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This is a continuation application claiming priority under 35 U.S.C. § 120 to U.S. application Serial Number 10/198,328, filed July 16, 2002, now abandoned which is a continuation of application U.S. Serial No. 09/669, 779, filed September 25, 2000, now U.S. Patent No. 6,469,047 B1, which claims priority under 35 U.S.C. § 119 to U.S. provisional application Serial No.60/156,062, filed September 24, 1999, the entire disclosures of which are hereby incorporated by reference.

## BACKGROUND OF THE INVENTION

The integrins are α/β heterodimeric cell surface receptors involved in numerous cellular processes from cell adhesion to gene regulation. Hynes, R.O., Cell, 1992, 69:11-25; Hemler, M.E., Annu. Rev. Immunol., 1990, 8:365-368. Several integrins have been implicated in disease processes and have generated widespread interest as potential targets for drug discovery. Sharar, S.R. et al., Springer Semin. Immunopathol., 1995, 16:359-378. In the immune system integrins are involved in leukocyte trafficking, adhesion and infiltration during inflammatory processes. Nakajima, H. et al., J. Exp. Med., 1994, 179:1145-1154. Differential expression of integrins regulates the adhesive properties of cells and different integrins are involved in different inflammatory responses. Butcher, E.C. et al., Science, 1996, 272:60-66. The alpha4 integrins (i.e. alpha4beta1 (α4β1) and alpha4beta7 (α4β7)) are expressed primarily on monocytes, lymphocytes, eosinophils, basophils, and macrophages but not on neutrophils. Elices, M.J. et al., Cell, 1990, 60:577-584. The primary ligands for α4 integrins are the endothelial surface proteins mucosal addressin cell adhesion molecule (MAdCAM) and vascular cell adhesion molecule (VCAM) with lower affinity. Makarem, R. et al., J. Biol. Chem., 1994, 269:4005-4011. The binding of the α4β7 or α4β1 to MAdCAM and/or VCAM expressed on high endothelial venules (HEVs) at sites of inflammation results in firm adhesion of the leukocyte to the endothelium followed by extravasation into the inflamed tissue. Chuluyan, H.E. et al., Springer Semin. Immunopathol., 1995, 16:391-404. Monoclonal antibodies directed against α4β1, α4β7, MAdCAM or VCAM have been shown to be effective modulators in animal models of chronic inflammatory diseases such as asthma (Laberge, S. et al., Am. J. Respir. Crit. Care Med., 1995, 151:822-829.), rheumatoid arthritis (RA; Barbadillo, C. et al., Springer Semin. Immunopathol., 1995, 16:375-379), colitis (Viney et al, J. Immunol., 1996, 157: 2488-2497) and inflammatory bowel diseases (IBD;